REMARKS

Claims

Claims 10–12 are currently under examination with claims 1–9 and 13–17 withdrawn from consideration due to restriction/election. Claims 18–19 are added by this paper.

Claim amendments

The claims have been amended according to conventional US practice. For example, use claim 13 has been amended to recite US process claim.

New claim 18 is supported by the disclosure contained in, for example, the ABSTRACT and page 1, lines 13–19 of the originally-filed specification. Support for new claim 19 can be found in original claim 9 and page 9, lines 5–7 of the originally-filed specification (i.e., an embodiment of the present invention relating to process for the preparation of such polypeptides by cultivation of a host organism and *isolation* of the corresponding polypeptide from the culture).

Applicants respectfully submit that the amendments presented herein do not raise new matter. Entry thereof is earnestly solicited.

Rejoinder

Withdrawn claim 13 is drawn to a method of *using* the compound(s) and/or composition(s) of the instant invention and recites all the elements of Applicants' product claims. "If a product claim is found allowable, process claims that depend from or otherwise require all the limitations of the patentable product may be rejoined." See M.P.E.P. § 806.05.

Rejoinder thereof is therefore respectfully requested.

Claim objections

The Examiner is thanked for her careful reading of the claims. The objection of claims 10 and 11 is moot in view of the amendment of the claims.

IDS

Copies of non-patent literature publications cited in the international search report (ISR) are enclosed herewith.

Rejection under 35 U.S.C. §112, ¶2

Claim 10 has been amended to use claim language in accordance with conventional US

practice. The issue of lack of antecedent basis is moot in view of the amendments.

Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §112, ¶1

Claims 10–12 are rejected due to allegedly lacking enablement with respect to the use of the polypeptides of the present invention as pharmaceutical compositions. This rejection is respectfully traversed.

Enablement

In the paragraphs bridging pages 5 and 8, the Office Action alleges that the pharmaceutical compositions are non-enabled. This contention is respectfully traversed.

Appellants' specification, coupled with a skilled worker's knowledge, provides more than adequate guidance on how to make the claimed polypeptide molecules and use pharmaceutical compositions and medicaments comprising such polypeptides for immunotherapy. The specification provides both general and specific guidance regarding the specific epitopes in allergens and how such could be manipulated for reliable hyposensitisation. See, for example, the disclosure contained in the paragraphs bridging pages 6 and 7 of the instant specification and the reference article by Schramm et al., 1999, J. Immunol. 162: 2406-2414. With respect to DNA vaccines, the specification explicitly teaches that "experimental evidence of allergen-specific influencing of the immune response has been furnished in rodents by injection of allergen-encoding DNA (Hsu et al., 1996, Nature Medicine 2 (5): 540-544)." Furthermore, the specification of the present application discloses specific immunotherapy or desensitization as therapeutic field for especially recombinant allergen proteins with higher purity and therefore reduced side effects than allergen proteins isolated from natural sources which are always mixtures of compounds. To this end, the specification discloses strategies to minimize the risks of side effects with the development of T-cell reactive fragments with reduced or no IgE-reactivity leading to hypoallergenic peptides (see, page 8, lines 15–26). The screening for T-cell and IgE epitopes were common knowledge at the priority date of the present application. Thus, a person skilled in the art would have been able to identify T-cell and IgE epitopes and produce hypoallergenic peptides. Nevertheless, also the classic approaches of specific immunotherapy and desensitization were applicable as a skilled person would have known the pharmaceutical effects and also the side effects and risks of an allergen protein administered to a patient and would have followed clinical recommendation protocols for specific immunotherapy and desensitization.

In relation to an enabling disclosure on the utilization of grass pollen allergen polypeptides in treatment of subjects, the specification provides a detailed disclosure for the design, synthesis and use of recombinant allergen extracts with reduced IgE reactivity. See, for example, the last paragraph on page 6 of the originally-filed specification. To this end, the Examiner is also courteously invited to review the disclosure contained in the enclosed Focke et al. (*FASEB Journal*, vol. 15, 2042-44, 2001). As evidenced by the disclosure in the "Immunization" section of Focke et al. and the immunoglobulin reactivity data provided in Figs. 5 and 6 and Tables 3–5 of the article, it is respectfully submitted that as of the filing date of the present application, the instantly claimed grass pollen allegens could be routinely manipulated and utilized as pharmaceutical preparations in a manner recited in the claims.

Thus it is respectfully submitted that the specification provides an enabling disclosure on the claimed allergenic properties of the recombinant, grass pollen allergen polypeptides of the instant invention. Therefore, the specification's express teaching that the claimed compounds are pharmaceutically useful is clearly credible as required. The PTO's contentions regarding non-enablement are especially weak in view of the detailed disclosure contained in Applicants' own specification and the state of the art before the earliest filing date of the instant application. Withdrawal of the rejection is respectfully requested.

To support the contention of non-enablement, the Office Action cites Tarzi (*Expert Opinion in Biol. Ther.*, 2003) to allege that "whole allergen immunotherapy is unpredictable." However, even Tarzi discloses the therapy of allergic diseases with specific immunotherapy or desensitization in general being effective and successfully applied for many years. See, the last paragraph at page 617 of the cited reference. Moreover, in Gefter et al. (USP 6,795,234), which was cited by the PTO in reference to an art rejection, the complete third and fourth paragraphs in the "BACKGROUND OF THE INETNION" (especially, col. 1, lines 26–45) discloses that the risk of systemic reactions like anaphylactic shock can be effectively minimized in individuals via specific immunotherapy, wherein pharmaceutical compositions comprising allergen polypeptides and/or vaccines comprising DNA sequences which encode such polypeptide allergens are utilized. As such, the PTO's contentions of non-enablement, based on the disclosure contained in Tarzi and/or Gefter is without merit.

The Office Action at page 6 alleges that it would "take undue trials and errors to practice the claimed invention." These allegations, however, do not present any evidence to doubt the objective enablement of Appellants' disclosure. As clearly and succinctly stated by the court in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> As a matter of Patent Office practice, then a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken in compliance with the enabling requirement of the first paragraph of §112, **unless** there is reason to doubt the objective truth of statements contained therein relied on for enabling support. (emphasis in original)

Furthermore, as stated in *Marzocchi*, at 370, the PTO must have adequate support (evidence or reasoning) for its challenge to the credibility of Appellants' statements of enablement. Thus, in the absence of evidence which demonstrates otherwise, the claims must be taken to satisfy the requirements of 35 U.S.C. § 112, ¶1.

Working examples are not required to establish enablement. As stated by the court *Marzocchi*, at page 369:

> The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

The assertion of undue experimentation in the rejection is merely conclusory. Further, as discussed above, the specification provides more than sufficient guidance to make and use the claimed medicaments and/or pharmaceutical compositions using no more than routine experimentation. Finally, a high level of skill does not establish that one skilled in the art would have reasons to doubt the veracity of the statements in Appellants' specification with respect to the use of the claimed composition in the diagnosis, treatment, and/or prevention of the claimed conditions.

Based on the aforementioned remarks and arguments, further in view of the amendments presented herein, it is respectfully submitted that Applicants' specification provides an enabling disclosure of what is claimed by the present invention. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

Rejections under §102

The art rejections under §102 are based on the references' disclosure of the term Lol p 4 polypeptide. The Office Action has not established that such polypeptides are structurally and/or identical to the polypeptide(s) encoded by SEQ ID NO: 1 or SEQ ID NO: 3, as claimed herein. More specifically, the totality of the disclosure in Bose (*Immunology*, 1998), Zhou (*Immunology*, 1995), Gefter (USP 6,759,234) or Gefter (WO 96/07428) says nothing about the identity of the polypeptides of the present invention which are currently claimed. Absent such, the references

cannot anticipate what is claimed herein.

The cited Gefter patent applications, Bose et al., Zhou et al, and the WO 96/07428 merely disclose in a Lol p 4 isolated from natural sources. Allergen protein isolated form natural sources are always mixtures of several compounds and allergens and isoforms thereof and never a pure form of the protein. This is the advantage of recombinantly prepared proteins and the inventors of the present invention were the first to clone and to determine the DNA sequence of Lol p 4. Thus, the DNA sequences in accordance with SEQ ID NO: 1 and 3 are not inherent in the reference Lol p 4 as the references do not disclose DNA molecules at all and also do not disclose amino acid sequences of a specific isoform of Lol p 4. The references are also silent with respect to recombinant polypeptides. See, the subject matter of the new claims. As such, the PTO's contentions are without merit.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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